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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/164,862	10/01/1998	PAUL A. PRICE	023070-08672	7170

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EXAMINER

UNGAR, SUSAN NMN

ART UNIT PAPER NUMBER

1642

DATE MAILED: 05/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

### Application No.

09/164,862

### Applicant(s)

PRICE ET AL.

### Examiner

Susan Ungar

### Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☐ Responsive to communication(s) filed on 20 October 2003 and 15 March 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☐ Claim(s) 1-18, 38, 39, 49-51 and 54-62 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☐ Claim(s) 1-18, 38-39, 49-51, 54-6 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- ☐ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_.
- ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: \_\_\_\_\_.

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1. The Amendment filed March 15, 2004 in response to the Office Action of October 15, 2003 is acknowledged and has been entered. The Amendment filed October 20, 2003 in response to the Office Action dated April 15, 2003 is acknowledged and has been entered. Previously pending claims 1, 38, 47 have been amended. Claims 1-18, 38-39, 49-51, 54-62 are currently being examined.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
3. The following rejections are being maintained:

***Claim Rejections - 35 USC 112***

4. Claims 1-18 remain rejected under 35 USC 112, first paragraph for the reasons previously set forth in the Office Action mailed October 15, 2003, Section 9, pages 4-9.

Applicant cites case law to demonstrate that the Court has indicated that the PTO's standard for meeting its burden of providing a reason to doubt the objective truth of the statements contained in the application to support an enablement rejection under 35 USC 112, first paragraph is the same standard as for establishing lack of utility under 35 USC 101. As drawn to the instant claimed invention, Applicant states that Examiner applies the same standards and suggests an inherently unbelievable undertaking or implausible scientific principles for the claimed invention.

It is noted for Applicant's information that the rejection of claims 1-18 under 35 USC 112, first paragraph is not a rejection under 35 USC 101 nor does it apply the same standards as for establishing lack of utility under 35 USC 101. The rejection clearly states that "Given the teachings of the specification and the art of record, it could not be predicted, with a reasonable expectation of success, that the

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invention would function as claimed” and thus one would be forced into undue experimentation to practice the claimed invention.

Applicant argues that Applicant’s invention is neither inherently unbelievable nor involves implausible scientific principles and specifically lists the characteristics of YKL-40 recognized by the Examiner. The argument has been considered but has not been found persuasive. Examiner never suggested or inferred that Applicant’s invention is inherently unbelievable nor involved with implausible scientific principles.

Applicant further argues that the specification teaches how to detect and measure YKL-40 levels and indicates typical YKL-40 levels in normal and diseased subjects, thus the specification teaches one of skill how to make and use the invention. The argument has been considered but has not been found persuasive because the issues raised here are not that the specification does not teach how to detect and measure YKL-40 levels or that YKL-40 levels are not indicated in normal and diseased subjects but rather that the claims are drawn to a method of estimating survival expectancy and that the Johansen et al paper upon which the teachings of the specification drawn to the breast cancer study appear to be based reveals that the sensitivity and specificity of a potential biochemical marker may vary considerably according to different cut-off values, that the number of patients in the present study is relatively small and further studies are needed and that although the study shows for the first time that determination of serum YKL-40 may play an important role for the prognosis of survival in patients suspected of breast cancer recurrence, the reference states that longitudinal studies relating serum YKL-40 to progression of breast cancer as well as in other cancer diseases and during different treatment procedures, are required. It is clear that

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Inventor Johansen agrees with Tockman et al of record as to the criteria required for a survival prognostic marker. It is further clear that neither the specification as originally filed nor the pilot study disclosed in the prior art reference enable the claimed invention in the absence of the studies specifically cited as necessary by both Johansen et al and Tockman et al. Finally, both the specification and the Johansen et al references make clear the unpredictable and speculative nature of the claimed invention with statements such as “if preoperative high levels of YKL-40 do prove to identify patients” (see specification) and “serum YKL-40 may play an important role...for the prognosis of survival in patients” (see Johansen et al).

Applicant further argues that (a) the invention is neither “inherently unbelievable” nor “involves implausible scientific principles” and (b) Examiner’s comments regarding the considerations necessary in bringing a cancer biomarker to successful clinical application are simply not applicable to analysis of the validity of the claims since *In re Brana* clearly teaches that usefulness in patent law and in particular in the context of pharmaceutical inventions necessarily includes the expectation of further research and development and the stage at which an invention becomes useful is well before it is ready to be administered to humans. The argument has been considered but has not been found persuasive because (a’) Applicant is reminded that the rejection set forth is drawn to lack of enablement and not lack of utility, (b’) *In re Brana* is not relevant as the claimed invention is not a pharmaceutical and is not to be administered. For the reasons of record, for the reasons clearly set forth by Inventor Johansen in the prior art reference, for the reasons set forth by Tockman, for the clear reasons drawn to the unpredictable and speculative nature of the claimed invention, the invention is not

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enabled. Applicant's arguments have been considered but have not been found persuasive and the rejection is maintained.

5. Claims 47, 49-51, 54-62 remain rejected under 35 USC 112, first paragraph for the reasons previously set forth in the Office Action mailed October 15, 2003, Section 10, pages 9-12.

Applicant argues that, with respect to Examiner's allegations regarding a nexus between conditions other than cancer and cancer with respect to elevated YKL-40 levels (a) there is no requirement to establish such a nexus because Applicant's have demonstrated a relationship between cancer diagnosis/prognosis and elevated YKL-40, (b) Applicant's have shown how to measure and assess YKL-40 levels and (c) Applicant reiterates arguments drawn to "inherently unbelievable" or "involves implausible scientific principles".

The arguments have been considered but have not been found persuasive because (a') contrary to Applicant's arguments, given that YKL-40 is elevated in the serum of patients with rheumatoid arthritis and liver disease, community-acquired pneumonia, inflammation of the arterial wall, bacterial meningitis, osteoarthritis, fibrosis, cirrhosis of the liver, in the absence of any nexus, it is not possible to determine or to predict whether the elevated YKL-40 found in the arthritis patients with inactive rheumatoid arthritis or the healthy woman patients were in any way associated with cancer. For the reasons of record, the invention is not enabled for prognosis, as to diagnosis, given the dozens of cancer types that are claimed wherein statistically significant difference between sample and control indicates the presence of cancer one would not know how to distinguish between the cancers or to distinguish the cancers one from the other and, given the many pathologies known to present with increased expression of YKL-40 it appears that

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even with the teaching of how to measure and assess YKL-40 levels, it would require undue experimentation to practice the claimed invention to determine whether one was identifying cancer or some other disease, (c') for the reasons set forth above.

Applicant argues that the amendment of claim 47 to recite that a "difference in YKL-40 level..... is an indicator of the presence of a cancer selected from a group of cancers obviates the instant rejection. The argument has been considered but has not been found persuasive for the reasons set forth above, that is that given the information in the specification and art of record, it is not possible to determine which disease the YKL-40 level is an indicator of or whether in a particular sample, the YKL-40 level is an indicator of cancer or any other of the diseases known to overexpress YKL-40. The arguments have been considered but have not been found persuasive and the rejection is maintained.

6. Claims 38-39 remain rejected under 35 USC 112, first paragraph for the reasons previously set forth in the Office Action mailed October 15, 2003, Section 12, pages 14-15.

Because Applicant did not distinctly and specifically point out the supposed errors in the rejection, the rejection is maintained.

7. Claims 1-18, 38-39, 49-51, 54-62 remain rejected under 35 USC 112, first paragraph for the reasons previously set forth in the Office Action mailed October 15, 2003, Section 13, pages 15-19.

Because Applicant did not distinctly and specifically point out the supposed errors in the rejection, the rejection is maintained.

8. All other objections and rejections recited in the Office Action mailed October 15, 2003 are withdrawn.

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9. No claims allowed.

10. This action is a **final rejection** and is intended to close the prosecution of this application. Applicant's reply under 37 CFR 1.113 to this action is limited either to an appeal to the Board of Patent Appeals and Interferences or to an amendment complying with the requirements set forth below.

If applicant should desire to appeal any rejection made by the examiner, a Notice of Appeal must be filed within the period for reply identifying the rejected claim or claims appealed. The Notice of Appeal must be accompanied by the required appeal fee.

If applicant should desire to file an amendment, entry of a proposed amendment after final rejection cannot be made as a matter of right unless it merely cancels claims or complies with a formal requirement made earlier. Amendments touching the merits of the application which otherwise might not be proper may be admitted upon a showing a good and sufficient reasons why they are necessary and why they were not presented earlier.

A reply under 37 CFR 1.113 to a final rejection must include the appeal from, or cancellation of, each rejected claim. The filing of an amendment after final rejection, whether or not it is entered, does not stop the running of the statutory period for reply to the final rejection unless the examiner holds the claims to be in condition for allowance. Accordingly, if a Notice of Appeal has not been filed properly within the period for reply, or any extension of this period obtained under either 37 CFR 1.136(a) or (b), the application will become abandoned.

11. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF



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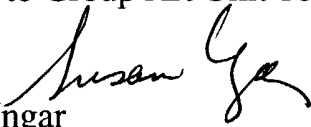
THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Ungar, PhD whose telephone number is (571) 272-0837. The examiner can normally be reached on Monday through Friday from 7:30am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan, can be reached at 571-272-0841. The fax phone number for this Art Unit is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Effective, February 7, 1998, the Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1642.

  
Susan Ungar  
Primary Patent Examiner  
May 19, 2004